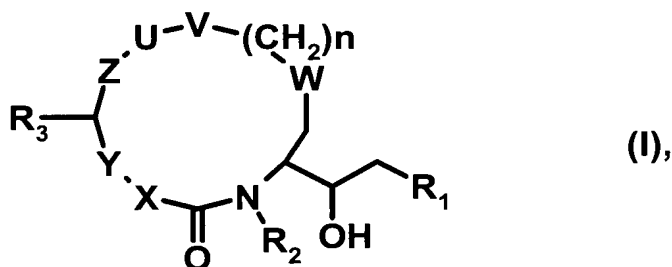


Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claim 1. (Currently amended): A compound of the formula



in which

R₁ is CH(R_c)C(=O)N(R_a)R_b or (CH₂)_kN(R_c)R_d, wherein

k is 0, 1 or 2;

R_a and R_b, independently, are hydrogen or an optionally substituted (C₁₋₈)alkyl, (C₃₋₇)cycloalkyl, (C₃₋₇)cycloalkyl(C₁₋₄)alkyl, aryl, aryl(C₁₋₄)alkyl, heteroaryl or heteroaryl(C₁₋₄)alkyl group,

R_c and R_d, independently, are hydrogen or an optionally substituted (C₁₋₈)alkyl, (C₃₋₇)cycloalkyl, (C₃₋₇)cycloalkyl(C₁₋₄)alkyl, aryl, aryl(C₁₋₄)alkyl, heteroaryl, heteroaryl(C₁₋₄)alkyl, chroman-4-yl, isochroman-4-yl, thiochroman-4-yl, isothiochroman-4-yl, 1,1-dioxo-1λ⁶-thiochroman-4-yl, 2,2-dioxo-2λ⁶-isothiochroman-4-yl, 1,2,3,4-tetrahydro-quinolin-4-yl, 1,2,3,4-tetrahydro-isoquinolin-4-yl, 1,2,3,4-tetrahydro-naphthalen-1-yl, 1,1-dioxo-1,2,3,4-tetrahydro-1λ⁶-benzo[e][1,2]thiazin-4-yl, 2,2-dioxo-1,2,3,4-tetrahydro-2λ⁶-benzo[c][1,2]thiazin-4-yl, 1,1-dioxo-3,4-dihydro-1H-1λ⁶-benzo[c][1,2]oxathiin-4-yl, 2,2-dioxo-3,4-dihydro-2H-2λ⁶-benzo[e][1,2]oxathiin-4-yl, 2,3,4,5-tetrahydro-benzo[b]oxepin-5-yl or 1,3,4,5-tetrahydro-benzo[c]oxepin-5-yl group, or

R_a and R_b, or R_c and R_d, together with the nitrogen to which they are attached, form an optionally substituted pyrrolidinyl, 1-piperidinyl, 4-morpholinyl or piperazinyl group; and

R_e is optionally substituted (C₁₋₈)alkyl, (C₁₋₄)alkoxy(C₁₋₄)alkyl, (C₃₋₇)cycloalkyl or (C₃₋₇)cycloalkyl(C₁₋₄)alkyl;

R₂ is hydrogen or (C₁₋₄)alkyl;

R₃ is hydrogen, (C₁₋₆)alkyl or an optionally substituted (C₁₋₆)alkylOC(=O)NH, (C₃₋₇)cycloalkylOC(=O)NH, (C₃₋₇)cycloalkyl(C₁₋₄)alkylOC(=O)NH, aryl(C₁₋₄)alkylOC(=O)NH, heteroaryl(C₁₋₄)alkylOC(=O)NH, (C₁₋₄)alkylC(=O)NH, (C₃₋₇)cycloalkylC(=O)NH, arylC(=O)NH, aryl(C₁₋₄)alkylC(=O)NH, heteroarylC(=O)NH or heteroaryl(C₁₋₄)alkylC(=O)NH group;

U is a bond, ~~CF₂, CF₂CF₂, CHF, CHFCHF, cycloprop-1,2-ylene, (C₁₋₃)alkylenoxy, (C₁₋₈)alkylene, NR_g or an aromatic or heteroaromatic ring, which ring is optionally substituted with halogen, (C₁₋₄)alkoxy, hydroxy or (C₁₋₄)alkyl, whereby Z and V are in ortho or meta position to each other, wherein~~

~~R_g is hydrogen, (C₁₋₈)alkyl or (C₃₋₇)cycloalkyl;~~

V is CH=CH, ~~cycloprop-1,2-ylene~~, CH₂CH(OH), CH(OH)CH₂ or CR_hR_hCR_hR_h, wherein each R_h, independently, is hydrogen, fluorine or (C₁₋₄)alkyl;

W is (C₁₋₆)alkylene, ~~O, S, S(=O)₂, C(=O), C(=O)O, OC(=O), N(R_f)C(=O), C(=O)NR_f or NR_f, wherein~~

~~R_f is hydrogen or (C₁₋₄)alkyl;~~

X is an optionally substituted (C₁₋₄)alkanylylidene ~~[[,]] or (C₁₋₄)alkylene, (C₃₋₇)cycloalkylene, piperidin-diyl, pyrrolidin-diyl, benzothiazole-4,6-diyl, benzoxazole-4,6-diyl, 1H-benzotriazole-4,6-diyl, imidazo[1,2-a]pyridine-6,8-diyl, benzo[1,2,5]oxadiazole-4,6-diyl, benzo[1,2,5]thiadiazole-4,6-diyl, 1H-indole-5,7-diyl, 1H-indole-4,6-diyl, 1H-benzimidazole-4,6-diyl or 1H-indazole-1,6-diyl group or an optionally substituted aromatic or heteroaromatic ring, whereby Y and C(=O)NR₂ are in meta position to each other;~~

Y is a bond, ~~O, S(=O)₂, S(=O)₂NR_g, N(R_g)S(=O)₂, NR_g, C(R_g)OH, C(=O)NR_g [[,]] or N(R_g)C(=O), C(=O)N(R_g)O or ON(R_g)C(=O), wherein~~

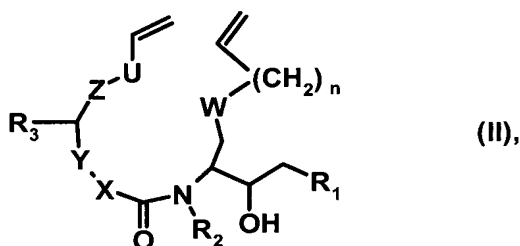
R_g is hydrogen, (C_{1-8}) alkyl or (C_{3-7}) cycloalkyl;

Z is ~~O, CH₂, CF₂, CHF, cycloprop-1,2-ylene~~ or a bond; and

n is 0 to 5,

the number of ring atoms included in the macrocyclic ring being 14, 15, 16 or 17, in free base form or in acid addition salt form.

Claim 2. (Original): A process for the preparation of a compound as defined in claim 1 of the formula I, in free base form or in acid addition salt form, comprising the steps of cyclisation by metathesis of a compound of the formula



in which R_1 , R_2 , R_3 , U, W, X, Y, Z and n are as defined for the formula I, in the presence of a catalyst, for instance a ruthenium, tungsten or molybdenum complex, optionally followed by reduction, oxidation or functionalisation of the resulting carbon-carbon-double bond, and of recovering the so obtainable compound of the formula I in free base form or in acid addition salt form.

Claim 3. (Canceled)

Claim 4. (Canceled)

Claim 5. (Original): A pharmaceutical composition comprising a compound as claimed in claim 1, in free base form or in pharmaceutically acceptable acid addition salt form, as active ingredient and a pharmaceutical carrier or diluent.

Claim 6-9. (Canceled)